REMARKS

The present paper is presented in response to the office action dated June 19, 2009. This paper is being filed with a petition and fee for a one-month extension of time to respond and as such, the response is timely filed on April 28, 2010.

A. Status of the Claims

Claims 21, 22, 24-26, and 32-37 were pending in the instant application. Claims 21, 22 and 24-26, and 32-37 were rejected under 35 U.S.C. 112 first paragraph for allegedly lacking enablement. Claim 32 was rejected for failing to comply with the written description requirement. Claims 21, 24 and 26 were rejected under was rejected under 35 U.S.C. 102(b) based on the disclosure of WO 92/21375 and claims 21, 24-25 and 26 were rejected under 35 U.S.C. 103 over a combination of WO 92/21375 and Moorman et al (J. Virology, vol 70, pages 763-770) and also in view of Drew et al.

B. Brief Description of the Subject Matter of Claims as Amended

In the amendment present above, Applicants have ensured that each of the claims recites a DNA sequence that encodes an infectious RNA virus. There are no claims directed to an isolated virus or an RNA sequence. The present application describes that the problem with plus strand RNA viruses is that:these viruses do not encompass a DNA step in their replication and as such in recombinant technologies, infectious clones i.e.,a DNA copy have to e developed before recombinant DNA techniques can be applied to generate the modified viruses. However, prior to the present invention these infectious clones were not generated because it was not known that the 5' end of the genome (in the

present claims the sequence of SEQ ID NO:18) was not known and this is a critical part of producing the infectious DNA sequence.

C. Rejection under 35 U.S.C. 112, first paragraph

Claim 32 was rejected for lack of written description under 35 U.S.C. §112, first paragraph. In the rejection, the Examiner noted that Claim 32 requires a full length infectious clone that expresses a heterologous Orf7 whereas Paragraph 18 of the specification describes a chimera that consists of a replaced Orf7. Applicants have amended claim 32 to insert the term "wherein the chimeric virus expresses the ORF 7 of PRSS strain ATCC VR2332 instead of the ORF 7 of PRSS strain CNCM I-1102". Applicants believe that insertion of the term "instead of the ORF 7 of PRSS strain CNCM I-1102" clarifies that the claim refers to the chimeric subject matter that is consistent with the disclosure at Paragraph 18 and with the written description requirement. Applicants respectfully request that the Examiner withdraw the rejection with respect to claim 32.

Claims 21, 22 and 24-26 were rejected under 35 U.S.C. 112 first paragraph as allegedly failing to comply with the enablement requirement. The Examiner noted that deposit of the strain consistent with the Budapest Treaty would satisfy the enablement requirement. Attached herewith is the Budapest Treaty Viability statement relating to PRRS virus strains deposited under accession number CNCM I-1102. Applicants believe this overcomes the rejection based on lack of enablement of claims 21, 22 and 24-26 and request that the rejection be withdrawn.

D. Rejection under 35 U.S.C. 102(b)

Claims 21, 24 and 26 were rejected under 35 U.S.C. 102(b) as anticipated by WO 92/21375. As noted above is section B the claims of the present invention relate to **an isolated DNA sequence** that encodes an infectious virus, moreover, claim 21, from which the remaining claims depend expressly recites that the DNA sequence comprises SEQ ID NO:18 at its 5' end. The Wensvoort et al reference WO 92/21375 fails to teach such a DNA sequence having SEQ ID NO:18 at its 5' end. While the WO 92/21375 provides a basic disclosure of the nucleic acid sequence of the RNA virus, the 5' sequence of SEQ ID NO:18 is not shown in WO 92/21375. That document states that:

> The nucleotide sequence of the genomic RNA of LV was determined from overlapping cDNA clones. A consecutive sequence of 15,088 bp was obtained covering nearly the complete genome of LV (Fig. 1). In this sequence 8 open reading frames (ORFs) were identified: ORF 1A, ORF 1B, and ORFs 2 to 7.

Importantly, however, the sequence of SEQ ID NO:18 (ATGATGTGTAGGG), which resides at the 5' end of the virus was not described in WO 92/21375. Claim 21 expressly recites "wherein said DNA sequence comprises SEQ ID NO:18 at the 5' end of the sequence of said PRRS virus strain". In the absence of that disclosure in Wensvoort, that reference cannot be used under 35 U.S.C. 102(b) for subject matter that describes a DNA sequence that produces an infectious clone. As such, the rejection of claims 21, 24 and 26 under 102(b) in view of Wenswoort et al should be withdrawn.

E. Rejection under 35 U.S.C. 103(a)

Claims 21, 22 and 23-31 were rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over WO 92/21375 in view of Moormann et al (J. of Virology, Vol 70 pp 763-770). In addition, the claims were rejected over a combination of WO 92/21375 in view of Moormann et al and in view of Drew et al. Applicants respectfully disagree with the Examiner and the following remarks apply to both the rejection based on WO 92/21375 in view of Moormann et al (J. of Virology, Vol 70 pp 763-770) and the rejection based on WO 92/21375 in view of Moormann et al (J. of Virology, Vol 70 pp 763-770) in view of Drew et al.

The claims as presented are directed to specific a cDNA infectious clones of PRRS virus strain deposited under accession number CNCM I-1102. As noted in the application, the use of such cDNA clones "circumvent[s] the problems encountered in viral RNA strand synthesis associated with the presence of incomplete viral RNA fragments." [para. 0013]. The specification teaches that "the utmost 5' end of the viral genome in genome length cDNA [creates] an infectious clone" [para. 0068] and that the presence of this 5' cap structure allowed the inventors to overcome the problems of producing the infectious clones.

WO 92/21375 provides the basic disclosure of the nucleic acid sequence of a PRRS virus strain. However, nowhere in WO 92/21375 is there a teaching that it would be desirable to include a specific sequence of SEQ ID NO:18 at the 5' end of the DNA sequence in order to be able to produce an infectious clone that encodes an RNA virus genome to render that clone infectious. Likewise, Moormann et al. fails to provide any guidance as to why a sequence of SEQ ID NO:18 as opposed to any other sequence would

be particularly useful in rendering a PRRS virus infectious. Drew et al. does nothing to supply this additional teaching. Thus, the teachings of the prior art are inadequate for rendering specifically claimed sequences obvious.

While the prior art, including WO 92/21375, may well have identified various PRRS viruses, as specifically noted in the specification, routinely infectious clones of such viruses were not described (page 10, ¶0029). It was the teachings of the present invention that showed that incorporating a sequence of SEQ ID NO:18 into the utmost 5' end into genome-length cDNA of those viruses to created infectious clones. With this teaching it is now possible to generate infectious isolated **DNA clones** of the PRRS viruses such that the DNA clones may be used to infect non-permissive host cells. As such, these isolated DNA sequences can be used to prepare infectious PRRS viruses in non-permissive cells and can then be used as delivery vehicles for generating an immune response. Wensvoort does not teach making infectious clones from DNA and Applicant respectfully submit that neither Drew et al. nor Moormann et al. show that in order to make an infectious DNA clone of a plus strand RNA virus such the PRRS virus CNCM I-1102 the skilled person would have to include in the cDNA sequence a sequence of SEQ ID NO:18. It is only by adding this sequence that the present inventors have been able to infect the DNA into a host cell that is not capable of being infected by a wild-type PRRS virus.

Moreover, as described in the present application at Paragraph 004, prior to the present invention the largest infectious clone produced was 12kb in length. Indeed, this is the length of the Pestivirus clone that is the subject of Moormann et al. This is too short a length for a full length PRRS virus genome which is an RNA sequence of about 15kb. In order to make an infectious clone of an RNA virus it is necessary to have a full-lgth reverse

transcript that includes the utmost 5' and 3' termini. The 5' terminus of SEQ ID NO:18 was only disclosed for the first time in the present application. The claims of the present invention for the first time describe an infectious DNA molecule which can be used in non-permissive cells to produce infectious PRRS virus clones.

In view of the above discussion and the amendment to the claims , Applicants believe the rejection of claims 21, 22 and 23-31 under 35 U.S.C. 103(a) should be withdrawn.

F. Closing Remarks

Applicants believe the above remarks and amendments overcome the outstanding rejections and Applicants request withdrawal of the rejections and reconsideration of the claims for allowance. No additional fees are believed to be due, however, should fees be deemed necessary or should there be an overpayment, the Commissioner is authorized to charge any additional fees or credit any overpayment to the Deposit Account of McAndrews, Held & Malloy, Account No. 13-0017.

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Respectfully submitted,

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